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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,772	11/06/2002	Noritsugu Yamasaki	06501-065001	5741

7590 09/24/2003
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EXAMINER

WRIGHT, SONYA N

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,772	YAMASAKI ET AL.	
	Examiner	Art Unit	
	Sonya Wright	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 4 is/are rejected.
- 7) ☒ Claim(s) 1-7 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 October 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>0903</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-7 are pending in this Office Action.

Election/Restrictions

Applicant's election without traverse of the species of compound number 14 at Figure 2 in the paper received August 1, 2003, is acknowledged. Applicants offer for consideration the following group, which encompasses the elected species:

drawn to compounds and compositions of formula I, wherein R1 represents an aryl lower alkyl group, said aryl group may be substituted with one or more groups selected from the group consisting of a halogen atom, an aryl lower alkyl group, an aryl lower alkenyl group, or an aryl lower alkynyl group; and R2 represents an aryl group which may be substituted with a lower alkyl group.

Claims 1-7 have been examined commensurate in scope with the group offered by Applicants (supra).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988)):

- 1) Nature of invention.
- 2) State of prior art.
- 3) Level of ordinary skill in the art.
- 4) Level of predictability in the art
- 5) Amount of direction and guidance provided by the inventor.
- 6) Existence of working examples.
- 7) Breadth of claims.
- 8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

1) Nature of the invention.

Claim 4 is directed to "a pharmaceutical composition for preventing and treating impaired glucose tolerance, diabetes, diabetic complications", etc. . . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

2) State of the prior art.

The prior arts do not indicate that the instant compound is useful in "preventing and treating" impaired glucose tolerance, diabetes, diabetic complications, etc. . . The specification does not cite any patents, journal articles, or other literature to support that

the instant indole derivative prevents and treats all of the diseases claimed in claim 4.

3) Level of ordinary skill in the art.

There are a vast number of diseases caused by impaired glucose tolerance, diabetes, diabetic complications, etc. . . , and Applicant does not give support for “preventing and treating” all forms of these disorders. The instant compounds have blood sugar level-depressing activity or PDE5-inhibiting activity. The level of ordinary skill in the art is high.

4) Level of predictability in the art.

Applicant provides a list of diseases on pages 1 and 2. However, the various forms of these disorders have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. Applicant does not discuss the differences between the diseases in said list. The art pertaining to impaired glucose tolerance, diabetes, diabetic complications, etc. . . remains highly unpredictable. For example, atherosclerosis is a form of arteriosclerosis characterized by atheromas of medium and large arteries, which can reduce or obstruct blood flow; glaucoma is characterized by increased intraocular tension and impaired vision; nephritis is characterized by hematuria, renal functional impairment, nerve deafness, and, sometimes, ocular abnormalities; allergic rhinitis is related to edema of the nasal mucous membrane; etc. . .

5) Amount of direction and guidance provided by the inventor.

Applicant provides limited guidance regarding industrial applicability on pages 51-52. Applicant provides limited information regarding biological activity on pages 49-

51. Applicant provides one test example, which is a test for activity of decreasing plasma glucose using db/db mice. Further, on pages 51-52, Applicant provides limited guidance regarding industrial applicability.

6) Existence of working examples.

Applicant provides one test example on pages 49-51, of a test for activity of decreasing plasma glucose using db/db mice. The results of the example were that when the test compound was administered at a dose of 3.2 mg/kg, plasma glucose decreasing activity was 19%, while TG concentration-decreasing activity was 9%. Claims 4 lists a large number of diseases and the test example does not enable the full scope of the claim.

7) Breadth of claims.

Claim 4 is extremely broad due to the large number of disorders encompassed by impaired glucose tolerance, diabetes, diabetic complications, etc. . . Applicant has not shown evidence that the instant compound is useful in "preventing and treating" all of said diseases.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not use the claimed invention without undue experimentation.

The attached articles support that lowering plasma glucose is useful in the treatment of diabetes: "DG DISPATCH –EASD: Pioglitazone Corrects Imbalance While

Lowering Plasma Glucose" Doctor's Guide Global Edition, Copywrite (c) 1995-Doctor's Guide Publishing Limited, and "Plasma Glucose Meters and Whole Blood Meters" Copywrite (c) 2003 by Joslin Diabetes Center.

In order to overcome this rejection, it is suggested that Applicant delete "preventing" from claim 4, limit claim 4 to the treatment of diabetes, and delete all other diseases listed claim 4.

Claim Objections

Claims 1-7 are objected to because of the following informalities:

Claim 4 does not indicate that a carrier is present with the composition.

Therefore, it is suggested that Applicant insert –and a pharmaceutically acceptable carrier— at the end of claim 4, after "claims 1 to 3" for proper form for a composition claim.

Claims 5-7 refer to an "aldehyde corresponding to R1" in step (a). The phrase "aldehyde corresponding to R1" is unclear. Based on the definition of R1 in claim 1, one cannot determine the metes and bounds of an "aldehyde corresponding to R1". For example, claim 1 indicates that R1 represents an aryl lower alkyl group. It is unclear if Applicant intends for "an aryl lower alkyl group" to be part of an aldehyde. Clarification is requested.

Claims 1-7 are objected to for containing non-elected subject matter. It is requested that Applicant limit the claims to the group supra, offered by Applicants. Appropriate correction is required.

Specification

The disclosure is objected to because of the following informalities:

The disclosure does not make reference to the continuing data. Therefore, it is requested that Applicant insert the following statement at the beginning of the specification, after the title: --This application is a 371 of PCT/JP99/01798 filed April 5, 1999.--

Appropriate correction is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sonya Wright, whose telephone number is (703) 308-4539. The examiner can normally be reached on Monday-Friday from 8:00 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (703) 308-4537. The Unofficial fax phone number for this Group is (703) 308-7922. The Official fax phone numbers for this Group are (703) 308-4556 or 305-3592.

When filing a FAX in Technology Center 1600, please indicate in the Header (upper right) "Official" for papers that are to be entered into the file, and "Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the

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applicant and should be addressed to [joseph.mckane@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-1235.

A handwritten signature in cursive script, reading "Joseph K. McKane", is positioned above a horizontal line.

Joseph K. McKane

Supervisory Patent Examiner

Group 1600

Sonya Wright

September 17, 2003